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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,426	03/25/2005	Ferdinand Hermann Bahlmann	P/2107-264	5804

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EXAMINER	
HEARD, THOMAS SWEENEY	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
06/23/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,426	BAHLMANN ET AL.	
	Examiner	Art Unit	
	THOMAS S. HEARD	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-107* is/are pending in the application.

4a) Of the above claim(s) *44,45,47-51,54-58,60-64,66-69,71-89 and 91-107* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46, 52, 53, 59, 65, 70, and 90* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/7/08 has been entered.

The Applicants Amendments to the claims received on 5/7/2008 is acknowledged. The text of those sections of Title 35 U.S. Code not included in the action can be found in the prior office action. Rejections or objections not addressed in this office action with respect to the previous office action mailed 1/8/2008 are hereby withdrawn.

Claim(s) 44-107 are pending. Applicants have not amended any claims. Claims 44, 45, 47-51, 54-58, 60-64, 66-69, 71-89, 91-107 are withdrawn. Claims 46, 52, 53, 59, 65, 70 and 90 are hereby examined on the merits.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

For the purpose of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. V. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held in accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw. In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties. In re Clinton, 188 USPQ 365, 367 (CCPA 1976);In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

Claims 46, 52, 53, 59, 65, 70, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fatouros MS et al "Influence of growth factors erythropoietin and granulocyte macrophage colony stimulating factor on mechanical strength and healing of colonic anastomoses in rats," Eur J Surg. 1999 Oct;165(10):986-92(from Applicant's IDS); Krussel JS, et al, "Vascular endothelial growth factor (VEGF) mRNA splice variants are differentially expressed in human blastocysts," Mol Hum Reprod. 2001 Jan;7(1):57-63, Amgen Inc, EP 0613683 A1; Zaharia Czeizler, US 6,274,158, and the new reference Westenfelder, US 6,748,154, for definition of subpolycythemic erythpoietin dosis and ranges.

The instantly claimed invention is drawn to a method for wound healing through the administration of a subpolycythemic erythropoietin (EPO) dosis and an ingredient that stimulates endothelial progenitor cells.

Fatouros MS et al teaches the administration of erythropoietin (EPO) which was shown to be beneficial for healing of colonic anastomoses (the joining and suturing of two sections of intestine in which the cut intestine is viewed as a wound), readable on Claim 46 and 90. Recombinant EPO was administered via subcutaneous injection, readable upon Claims 52 and 53. Fatouros MS does not teach a weekly subpolycythemic erythropoietin (EPO) dosis of 1 to 90 IU of EPO/kg, pulmonary administration of EPO, oral administration of EPO, or an additional ingredient that stimulates endothelial progenitor cells.

Westenfelder, US 6,748,154, the definition of subpolycythemic erythpoietin dosis and ranges as being about 250-350 U/kg body weight, indicating that ranges less than this do not induce polycythemia, see column 6 and line 45 onward for example.

Zaharia Czeizler, US 6,274,158 further teaches the oral, subcutaneous, and intravenous administration of EPO for the treatment of bleeding due to surgical treatments (wounds made by the surgical process), for example, see abstract and claim 32 for example. Amgen Inc, EP 0613683 A1, teaches EPO may be formulated for inhalers (Pulmonary administration), see abstract. Zaharia Czeizler and Amgen's references are readable upon Claims 59, 65, and 90.

Krussel JS, et al teaches the compound VEGF (vascular endothelial growth factor) stimulates endothelial progenitor cells and induces angiogenesis, see Introduction and column 2, readable on Claim 70. Applicants have define wound healing as: "*In connection with the present invention, 'wound healing' means the physiological processes for regenerating damaged tissue and for closing a wound,*

especially formation of new connective tissue and capillaries." Therefore, VEGF is viewed as a compound that not only is a compound that induces angiogenesis (capillary formation) but is also a compound that heals wound by Applicant's definition

The difference between what is taught by the prior art and that instantly claimed is that while Fatouros MS et al does not teach subpolycythemic erythpoietin dosis, Westenfelder teaches the subpolycythemic erythpoietin dosis ranges but does not teach a single subpolycythemic erythpoietin dosis.

It would have been obvious at the time of instantly claimed invention to use EPO for the purposes and benefits of wound healing. It would also have been obvious to use EPO in combination with VEGF for wound healing as it is obvious to combine two compositions to form a third composition that performs the same function. One would have been motivated to do so given Fatouros' clear teaching of wound healing properties of EPO and Krussel's teaching that VEGF induces angiogenesis, an important part of wound healing from Applicant's definition of wound healing. Although Fatouros does not teach a method of using a composition comprising the specifically claimed concentration of the compounds for wound healing and at the particular dosage of 1 to 90 IU EPO/kg, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have optimized the concentration for administration of EPO for different wounds and different formulations and routes of administration taught by the references supra.

Where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Applicant's arguments have been carefully considered but are not held to be persuasive to overcome the rejection. Applicants argue that the dosages as taught by the references are all above the ranges claimed and administered to the subject. It is further argued that because these higher ranges are taught that it is a teach away from lower concentrations. Further, there appears in the teachings that high doses also cause high blood pressure and other (unnamed) physical manifestation known in the art. Applicants have also provided arguments under 37 C.F.R. 1.132, but will not be addressed here but below specifically addressing the declaration.

The arguments provided by the Applicants are not persuasive for a number of reasons. First, the nexus between wound healing and EPO has been established and given this connection, it is but routine optimization to find the optimal concentrations for the desired effect with minimizing unwanted side effects or for purposes of cost reduction:

For the purpose of this invention, the level of ordinary skill in the art is deemed to be at least that level of skill demonstrated by the patents in the relevant art. Joy Technologies Inc. V. Quigg, 14 USPQ2d 1432 (DC DC 1990). One of ordinary skill in the art is held in accountable not only for specific teachings of references, but also for inferences which those skilled in the art may reasonably be expected to draw.

In re Hoeschele, 160 USPQ 809, 811 (CCPA 1969). **In addition, one of ordinary skill in the art is motivated by economics to depart from the prior art to reduce costs consistent with desired product properties**. In re Clinton, 188 USPQ 365, 367 (CCPA 1976);In re Thompson, 192 USPQ 275, 277 (CCPA 1976).

Given Westenfelder' teaching that EPO can cause polycythemia would lead one of ordinary skill in the art to at least explore the ranges below what is considered a subpolycythemic erythpoietin dosis. Further, one of ordinary skill in the art knows that nearly all drugs or natural products have a level that has a deleterious effect on the subject, the optimal range is sought to minimize the side effects while providing a benefit. It should be noted that while aspirin can treat a headache, it also can cause bleeding. While chemotherapy can cause anemia, the anemic patient can be cured of the tumor and live to restore his or her blood count. Would healing is generally a short process and, absent evidence to the contrary, it is doubtful that a therapeutic regime for wound healing would induce high blood pressure in that time period to the point of avoiding EPO therapy. It is of interest to the pharmaceutical industry to determine the optimal dose of any drug for both economic and health benefit purposes, as weel as convenience of delivery for the patient in need. Applicants arguments of the prior art teaching higher concentrations and/or high EPO concentration causing high blood pressure are not persuasive to overcome the rejection as the nexus between EPO and wound healing has been established and it is the Examiner's position that it is only routine optimization to arrive at the instant invention. Therefore, the rejection stands for the reasons stated supra.

Response to Amendment

The declaration under 37 CFR 1.132 filed 5/7/2008 is insufficient to overcome the rejection of Claims 46, 52, 53, 59, 65, 70, and 90 based upon 35 USC § 103 as set forth in the last Office action. There are two 37 CFR 1.132 declarations, one from Hermann Haller and one from Ferdinand Herman Bahlmann. Except for the different names and inconsistencies in the provided graph, the declarations are identical. Applicants have argued the lower dosage led to a complete closing after 7-8 days when compared to the higher dosage. This is not convincing for a number of reasons. First, there is no day seven on the graph. On day 8 there is a difference between the control, the EPO 20 IU/kg/wk, and 200 IU/kg/wk, but there are no error bars to provide any relevance to the data points. Applicants are stating that on day seven or eight there is complete closure of a small wound. The value that is associated with this closure, or a range of values associated with the closure is not stated. It appears that there is little difference between day 8 and onward between the control or the other two doses, and without error bars, the differences approaching day seven or eight cannot be evaluated. Day four and six appear aberrant without error bars and statistical considerations cannot be made to access the quality of the data. Even so, the rate of healing does not appear to be significant for the EPO 20 IU/kg/wk over the control and the dramatic change in the EO 200 IU/kg/wk between day 6 and day 8 are not believable without statistics and appear to be an anomaly because the change is approximate what was observed for the EPO 20 IU/kg/wk for day zero through day 6! It is the examiners position that the evidence provided has not shown substantial evidence that there is an

improvement in the dosing to warrant the invention to be free of the prior art. Therefore the rejection stands.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 46, 52, 53, 59, 65, 70, and 90 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 4, 15-31, 35-44 of copending Application No. 10/586,896. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant Application is drawn to the use of EPO for the purpose of wound healing. The 10/586,896 Application is drawn to the use of (which the Examiner is interpreting to mean a method of) EPO for the treatment of wound, specifically wound healing in addition to a combination therapy of EPO with VEGF. Oral, parenteral, and pulmonary (aerosol) administration are also claimed.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicants have argued:

As previously noted by applicants in their response dated November 26, 2007, the M.P.E.P. indicates (see §8041 B) that in the case of provisional obviousness-type double patenting rejections based on the claims of copending applications (as in the present instance): The 'provisional' double patenting rejection should continue to be made by the Examiner in each application as long as there are conflicting claims in more than one application unless that 'provisional' double patenting rejection is the only rejection remaining in at least one of the applications. (Emphasis supplied by applicants). Applicants respectfully submit that the arguments and evidence set forth above is believed to be clearly sufficient to overcome the § 103 rejection of applicants' claims. Thus, the 'provisional' obviousness-type double patenting rejection should be "the only rejection remaining in" the present application. This factor, thus, should lead to the withdrawal of the double patenting rejection. The Examiner is, therefore, respectfully requested to also reconsider and to withdraw the double patenting rejection of applicants' claims.

The arguments stated supra have not overcome the rejection and the ODP stands.

Conclusion

No claims are allowed.

Applicant should specifically point out the support for any amendments made to the disclosure, including the claims (MPEP 714.02 and 2163.06). Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Thomas S. Heard whose telephone number is (571) 272-2064. The examiner can normally be reached on 9:00 a.m. to 6:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Thomas S Heard/
Examiner, Art Unit 1654

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654